IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Application No. 10/562,776

Confirmation No. 7650

Applicant: Kuroita et al.

Filed: December 29, 2005

TC/AU: 1641

Examiner: Lisa V. Cook

Docket No.: 248832 (Client Reference No. 2005AE/US)

Customer No.: 23460

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL OF DECLARATION UNDER 37 C.F.R. § 1.131

Dear Sir:

Applicants submit herewith an executed Declaration under 37 C.F.R. § 1.131 for the above-referenced application and respectfully request that the same be made of record in the above-identified patent application.

The Commissioner is hereby authorized to charge any fees that may be required for this submission or credit any overpayment, to Deposit Account No. 12-1216.

Respectfully submitted,

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Date: March 13, 2009

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DECLARATION UNDER 37 C.F.R. § 1.131

We, Toshihiro Kuroita, Atsushi Sogabe, Yutaka Takarada, and Naoki Tanaka do hereby declare that:

1. We are the inventors of the subject matter disclosed and claimed in the above-described application.

2. We conceived of and reduced to practice the claimed invention before July 12, 2003, which corresponds to the online publication date of Chesnokova et al., *Biochemistry, 42*: 9028-9040 (2003).

3. As merely an example of both the conception and reduction to practice of the claimed invention, attached hereto is an English translation of the relevant portion (i.e., the portion showing support for the claimed invention) of Japanese Patent Application 2003-191081, filed July 3, 2003, to which the above-identified application claims priority.

4. We hereby declare that all statements made herein of our own knowledge are true, that all statements made on information and belief are believed to be true, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: March 11, 2009

Toshihiro Kuroita

Toshihiro Kuroita

Date: March. 11, 2009

Atsushi Sogabe

Atsushi Sogabe

Date: March. 11, 2009

Yutaka Takarada

Yutaka Takarada

Date: March. 12. 2009

Naoki Tanaka

Naoki Tanaka

VERIFICATION OF TRANSLATION

Re: JAPANESE PATENT APPLICATION NO. 2003-191081

I, Masaki MORISHIMA, of Kitahama TNK Building, 7-1, Dosho-machi 1-chome, Chuo-ku, Osaka-shi, Osaka 541-0045, Japan hereby declare that I am the translator of the document attached and certify that the following is true translation to the best of my knowledge and belief.

Signature of translator 

Masaki MORISHIMA

Dated this 10th day of March, 2009

English translations of the relevant portion of Japanese Patent Application 2003-191081

1. English translation of a part of paragraph [0001] in JP2003-191081, which is relevant to page 1, lines 10-13 in the originally filed specification of US application 10/562,776

"The present invention also relates to a blocking reagent, a stabilizing agent, an excipient, a protein folding accelerator, a protein refolding accelerator and a coating agent for medical use, which contain the protein."

2. English translation of a part of paragraph [0045] in JP2003-191081, which is relevant to page 22, lines 17-19 in the originally filed specification of US application 10/562,776

"Preferably, a substrate-binding domain of the HSP 70 family protein from which an ATPase domain has been deleted is preferably used, and more preferably, the substrate-binding domain of the DnaK protein of *Escherichia coli* from which an ATPase domain has been deleted is used."

3. English translation of a part of paragraph [0047] in JP2003-191081, which is relevant to page 23, lines 1-9 in the originally filed specification of US application 10/562,776

"In particular DnaK in *Escherichia coli* has been well-studied, and thus, it can be said that it is relatively easy to predict the effect of the amino acid modification. This protein is composed of 638 amino acid residues, and comprised of an "ATPase (ATP-binding) domain" composed of the amino acids at positions 1 to 385 and a "substrate-binding domain" composed of the amino acids at positions 386 to 638 (Fig.6). The sequence of the DnaK protein is shown in SEQ ID NO:1, and its gene sequence is shown in SEQ NO:2."

4. English translation of a part of paragraph [0050] in JP2003-191081, which is relevant to page 23, line 23 - page 24, line 6 in the originally filed specification of US application 10/562,776

"First, we attempted to make the protein excellent in blocking efficiency by adding the mutation to a β sheet structure portion to enhance the

hydrophobicity in the β sheet portion. The attempt is that (1) a more hydrophobic portion of the β sheet is exposed by deleting a part of the N terminus of the β sheet (the β sheet structure is broken to enhance the hydrophobicity) and (2) a hydrophilic amino acid in the β sheet is substituted with a hydrophobic amino acid. As a result, remarkable enhancement of the blocking efficiency could be observed in DnaK 419-607 where the N terminal portion of the β sheet structure had been deleted and DnaK 384-607 (D479V, D481V) where the hydrophilic amino acid had been substituted with the hydrophobic amino acid (Fig. 9). This time especially, the remarkable enhancement of the blocking efficiency was observed in DnaK 419-607. It appears that this protein exhibits the blocking in a form shown in Fig. 8. That is, it is thought that by changing the structure of the hydrophobic domain, the structure of the hydrophobic domain was changed to enhance the hydrophobicity of the hydrophobic domain, which was conductive to the enhancement of the blocking ability."

5. English translation of paragraph [0053] in JP2003-191081, which is relevant to page 24, lines 17-23 in the originally filed specification of US application 10/562,776

"Discussing the reason why the efficiency was remarkable in DnaK 419-607 in more detail, it is speculated that the efficiency is caused by exposing outside a part of an inside of a horseshoe shaped structure which is hydrophobicity-rich for trapping a peptide as a substrate of a chaperone by removing the β sheet portion adjacent to a hinge portion of the horseshoe shaped structure of the DnaK substrate-binding domain."

Fig. 6

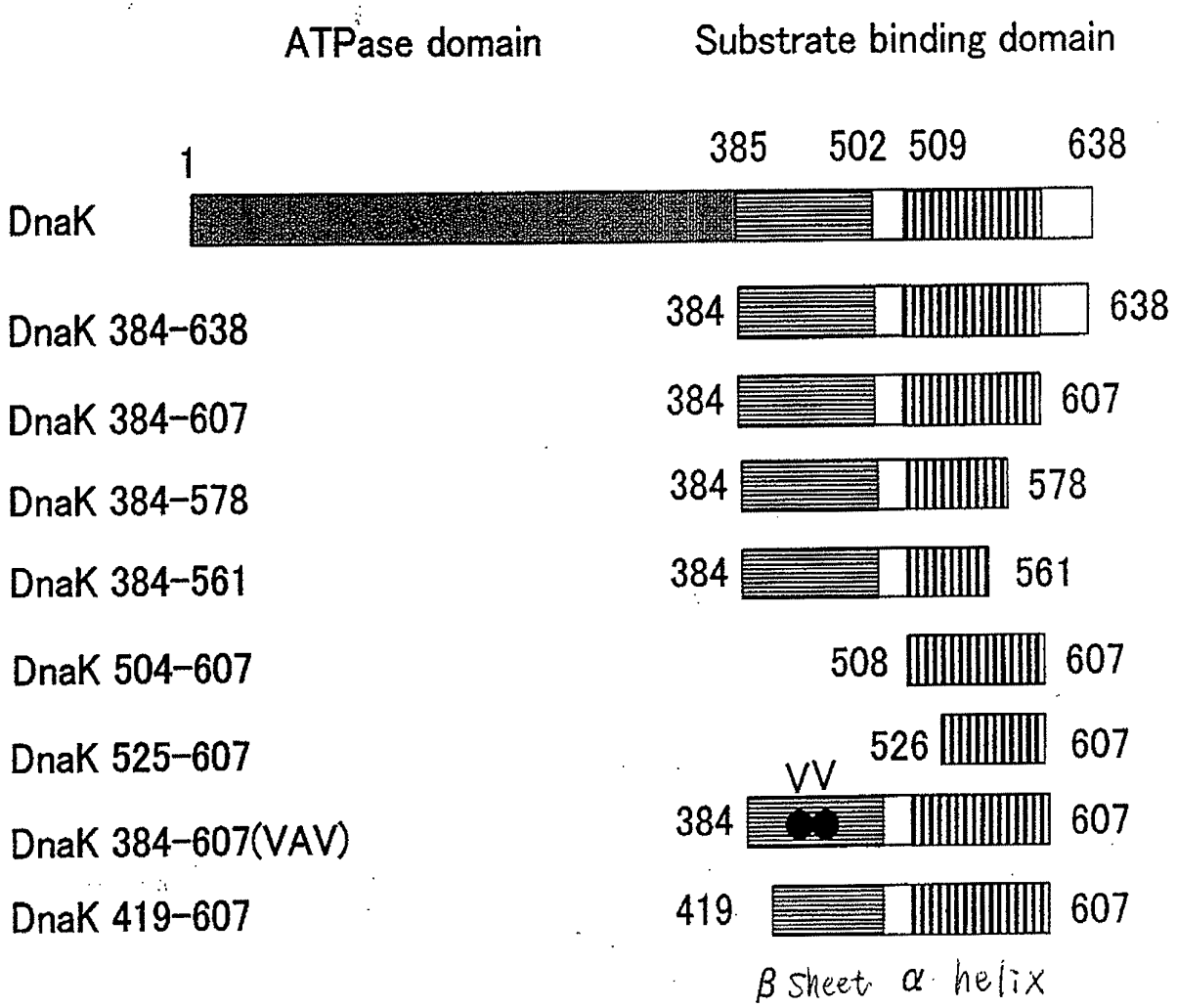
ATPase domain
Substrate binding domain
1
385
502
509
638
DnaK
DnaK 384-638
384
638
DnaK 384-607
384
607
DnaK 384-578
384
578
DnaK 384-561
384
561
DnaK 504-607
508
607
DnaK 525-607
526
607
VV
DnaK 384-607(VAV)
384
607
DnaK 419-607
419
607
β sheet
α helix

Fig. 9